Appl. No. 09/653,563 Amdt. Dated September 2, 2005 Reply to Office Action of July 29, 2005

## REMARKS/ARGUMENTS

This communication is responsive to the Office Action dated July 29, 2005, having a period of response through October 29, 2005.

Claims are deleted which brings the total number of claims to eight (8) independent claims. No new matter has been added.

Claims 1, 21 and 157-191 were pending. After entry of the above amendment, Claims 170-171, 175-176, 185-186 and 190-191 will still be pending.

This amendment deletes claims 1, 21 157-169, 172-174, 177-184 and 187-189 as being drawn to a non-elected invention and leaves claims 170-171, 175-176, 185-186 and leaves claims 190-191 as previously presented.

Applicants acknowledge allowance of claims 170, 175, 185 and 190.

## Rejections Under 35 U.S.C. §§ 112

Claims 171, 176, 186 and 191 stand rejected under 35 U.S.C. §§ 112, first paragraph, as failing to comply with the written description requirement. The Examiner asserts that the claims contain the subject matter "treating bone pain associated with bone cancer" was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicants traverse this part of the rejection and respectfully request withdrawal of the same.

The Examiner's attention is directed to the paragraph bridging page 791 line 24 and page 792, line 4 of the specification which recites inter alia, "[t]he compounds of the present invention are useful (in a human or other mammal) for the treatment of ... bone pain associated with bone cancer."

Claims 171, 176, 186 and 191 also stand rejected under 35 U.S.C. §§ 112, first paragraph, because the specification, while being enabling for the instant compounds for treating nociception, does not reasonably provide enablement for the instant compounds for treating bone pain associated with bone cancer. The Examiner further asserts that the specification does not enable any person skilled in the art to which it pertains, and with which it is most

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nearly connected, to use the invention commensurate in scope with these claims.

Applicants also traverse this part of the rejection and respectfully request withdrawal of the same.

The Examiner's attention is directed to page 769 lines 20-21 of the specification, which states "[S]tudies were performed on patients with asymptomatic hormone refractory prostate cancer with rising PSA levels and on male subjects with symptomatic hormone refractory prostate cancer with rising PSA levels and pain (emphasis added)."

The Examiner's attention is also directed to page 775 line 6 to page 776 line 17 where the skeletal involvement of cancer that has metastasized from the prostate (primary) cancer to bone is discussed.

The Examiner's attention is also directed to page 774 line 15 to page 775 line 3 where inhibition of IL-6 inhibition and accompanying reduction of inflammation and amelioration of pain due to the bone cancer is discussed.

Finally, the Examiner's attention is directed to page 776 line 20 to page 779 line 6 where the VAS methodology for subjective pain assessment and the therapeutic utility of a specific endothelin receptor are discussed.

These data support Applicants' assertion that bone pain associated with bone cancer may be ameliorated by treatment with the species recited in claims 171, 176, 186 and 191.

## CONCLUSION

Allowance of claims 170-171, 175-176, 185-186 and 190-191 is respectfully requested.

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